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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,583	11/24/2003	Moshe Bentolila	225326	5052

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding..

Office Action Summary	Application No.	Applicant(s)	
	10/720,583	BENTOLILA ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are pending.

Specification

The use of the trademarks PROVIGIL® (pg. 1-3, 6, and 8-10), MODIODAL® (pg. 1), and VIGIL® (pg. 1) have been noted in this application. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2-4, 6, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 3 are vague and indefinite, because it would not be apparent to a person of ordinary skill in the art in which solvent and temperature the pharmaceutical composition is characterized by dissolution of a given percentage of said composition within a specified period of time.

Claims 4, 6, and 14 are vague and indefinite because trademarks do not refer to a specific composition. The manufacturer of goods and services associated with a particular trademark could modify said goods/services and thereby inherently change any properties associated with said products/services. The use of trademarks in a claim to refer to a product is improper as stated in the MPEP § 2173.05 (u).

Claim Rejections - 35 USC § 102

Claims 1-4 and 6, 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Grebow et al. (U.S. Patent No. 5,618,845) ("USPN '845").

The Applicant claims an oral pharmaceutical composition comprising modafinil particle sizes, wherein at least ***about 5%*** of said modafinil particles have a diameter greater than 200 microns, and wherein said composition has properties similar to those of PROVIGIL® tablets.

It is noted that UPSN '845 is owned by the manufacturer of commercially available modafinil compositions, associated with the trademark PROVIGIL®.

Grebow discloses an acetamide derivative (**modafinil**) having a defined particle size, which can have a significant effect on the potency and safety profile of the drug (title and abstract).

Grebow discloses that the word "about" means plus or minus approximately ten percent of the indicated value (col. 2, lines 44-49). Grebow also discloses that it is preferable that not more than **about 5%** of the cumulative total (percent cumulative) of modafinil particles in any one dose provided to a mammal have particle sizes greater than **about 200 microns** (col. 3, lines 16-20). About 5% includes amounts ranging from 4.5% to 5.5% and about 200 microns includes

particle sizes ranging from 180 microns to 120 microns. Therefore, the amounts of particles having a particle size greater than 200 microns as disclosed by Grebow overlaps with the range in the amount of particles having a particle size greater than about 200 microns as recited by the Applicant in claim 1 of the instant application.

Grebow discloses that the pharmaceutical composition can contain **at least about 50 mg** (i.e. 45-55 mg), preferably at least **about 100 mg** (i.e. 90-110 mg), or **more preferably at least about 200 mg** (i.e. 180-220 mg) of modafinil having a particle size as defined previously (col. 4, lines 11-15). In Table 1, Grebow discloses the mean and median particle diameters of modafinil compositions from "early lots (designated as E-Letter)" and "later lots (designated as L-#)," including compositions having a **median particle size greater than 60 and greater than 90 microns** (i.e. entries E-A to L-1 in Table 1).

Grebow discloses that his invented modafinil compositions are preferably **administered orally** in the form of a vehicle such as a **tablet, capsule, powder**, pill, liquid/suspension or emulsion. The carrier may also comprise agents that aid solubility, absorption, flavor, color or texture of the vehicle or its contents (col. 10, lines 18-24).

Regarding the rate of dissolution of Grebow's disclosed pharmaceuticals in comparison with those recited by Applicant, the Examiner concludes that Grebow's compositions inherently meet these limitations, because the prior art discloses a composition having the same components and a composition is inseparable from its properties. This assertion is further supported by Applicant's Figures 1-2, wherein the dissolution properties and the resulting blood plasma concentration of Applicant's administered composition are compared to the commercially

available product associated with the PROVIGIL® trademark, and appear to be the same within experimental error.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grebow et al. (U.S. Patent No. 5,618,845) ("USPN '845").

Applicant Claims

The Applicant claims an oral pharmaceutical composition comprising modafinil particle sizes, wherein (a) at least ***about 5%*** of said modafinil particles have a diameter greater than 250 microns (claim 7), (b) at least ***about 10%*** of said modafinil particles have a diameter greater than 200 microns (claim 8), and (c) at least ***about 15%*** of said modafinil particles have a diameter greater than 190 microns (claim 9).

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Many of the teachings of the prior art have been set forth above in the previous rejection of claims 1-4 and 6, 10-14 made under 35 U.S.C. §102(b) as being anticipated by Grebow et al. (U.S. Patent No. 5,618,845) ("USPN '845"). Additional relevant teachings are set forth below.

Grebow teaches in section VII, entitled "Effect of Modafinil Particle Size on Modafinil Plasma Concentration" that the results of animal studies with dogs led them to conclude that it was important to control modafinil particle size to address safety concerns and the use of modafinil particles having a defined size is more efficient because a given plasma modafinil concentration can be achieved at a lower oral dose (col. 9, lines 37-47).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

The difference between the prior art teachings and the recited claims of the instant application is that the instant Application recites larger particle sizes and a greater amount of said particles having a larger particle size than what is generally preferred by the prior art reference.

Although the prior art does teach a preference for smaller particles sizes, it would have been obvious to a person of ordinary skill in the art at the time of the instant application that the size of particles in an oral composition and the amount of active agent in a composition are parameters that one would optimize. The physical characteristics (e.g. size and shape) and of particulate compositions as well as the amount of ingredients in a composition are clearly result specific parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal physical characteristics (e.g. particle size.) and the amount of different ingredients of a particulate composition needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. This is further evidenced by Applicant's figures 1-2, wherein the compositions of the instant application and those of the prior art have essentially the same dissolution properties and result in the same modafinil plasma concentration profiles.

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heacock et al. (U.S. 2004/0048931) ("Heacock").

Applicant Claims

The Applicant claims an oral pharmaceutical composition comprising modafinil particle sizes, wherein (a) at least ***about 5%*** of said modafinil particles have a diameter greater than 250 microns (claim 7), (b) at least ***about 10%*** of said modafinil particles have a diameter greater than 200 microns (claim 8), and (c) at least ***about 15%*** of said modafinil particles have a diameter greater than 190 microns (claim 9), wherein said compositions have properties similar to those of PROVIGIL® and are 80% dissolved within 30 minutes and 50% dissolved within 10 minutes.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Heacock teaches pharmaceutical compositions comprising modafinil in the form of particles of defined size (abstract). These compositions may comprise particles selected from discrete lots; including a small particle size lots (sizes ranging from less than or equal to 0.1 microns to less than or equal to 200 microns), large particle size lots (sizes ranging from less than or equal to 220 microns to less than or equal to 400 microns), and very large particle size lots (sizes ranging from less than or equal to 400 microns to less than or equal to 500 microns) [0029] through [0031]. Compositions comprising different sized modafinil particles are taught in Examples 3-42 and tabulated in column 9, including compositions comprising particles wherein (a) **20% of the particles have a size of equal to or less than 200 microns** (Ex. 9) and (b) **0-5% of the particles have a size less than or equal to 400 microns** (Ex. 11).

Heacock notes that routine experimentation is desirable to determine optimum particle size makeup and proportions or mixtures that exhibit similar dissolution profiles and/or are

bioequivalent to commercially available modafinil associated with the PROVIGIL® trademark [0064].

Heacock also teaches that the compositions may further comprise surfactants, including non-ionic, ionic, and bile salt surfactants such as sodium alkyl sulfates (ionic), polyoxyethylene sorbitan fatty esters (non-ionic), and deoxycholic acid (bile salt) [0066]. The term "surfactant" reads on the term "dissolution modifier," per Applicant's description of what constitutes a dissolution modifier on page 3 of the instant specification. Heacock's invented modafinil compositions are preferably administered orally in the form of vehicles such as tablets, capsules, powders, pills, etc. [0069].

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

The difference between the prior art teachings and the recited claims of the instant application is that the instant Application recites "a dissolution modifier" in claim 5 and that the compositions of the instant application have specific dissolution profiles after a specified period of time and properties comparable to the commercially available modafinil composition associated with the PROVIGIL® trademark.

Although the prior art does not expressly teach a "dissolution modifier" per se, it would have been apparent to a person of ordinary skill in the art at the time of the instant invention that surfactants are dissolution modifiers, as evidenced by Applicant's disclosure on page 3 of the instant application. Regarding the dissolution profiles and other properties of Applicant's recited composition, it would have been apparent to a skilled artisan that the prior art composition would have the same or a substantially similar dissolution profile and properties intrinsically associated

with solid oral modafinil compositions, because the prior art teaches the same composition as that recited in the claims of the instant application.

Other Matter

The Examiner respectfully suggests inserting the words "particle size" between the words "median" and "of" in claim 10, line 2, as this would remove any ambiguity as to what "median" Applicant is referring.

Conclusion

Claims 1-14 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0664. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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